



## **Estimating the risk of PTSD in recent trauma survivors: results of the International Consortium to Predict PTSD (ICPP)**

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# Estimating the risk of PTSD in recent trauma survivors: results of the International Consortium to Predict PTSD (ICPP)

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*A timely determination of the risk of post-traumatic stress disorder (PTSD) is a prerequisite for efficient service delivery and prevention. We provide a risk estimate tool allowing a calculation of individuals' PTSD likelihood from early predictors. Members of the International Consortium to Predict PTSD (ICPP) shared individual participants' item-level data from ten longitudinal studies of civilian trauma survivors admitted to acute care centers in six countries. Eligible participants (N=2,473) completed an initial clinical assessment within 60 days of trauma exposure, and at least one follow-up assessment 4-15 months later. The Clinician-Administered PTSD Scale for DSM-IV (CAPS) evaluated PTSD symptom severity and diagnostic status at each assessment. Participants' education, prior lifetime trauma exposure, marital status and socio-economic status were assessed and harmonized across studies. The study's main outcome was the likelihood of a follow-up PTSD given early predictors. The prevalence of follow-up PTSD was 11.8% (9.2% for male participants and 16.4% for females). A logistic model using early PTSD symptom severity (initial CAPS total score) as a predictor produced remarkably accurate estimates of follow-up PTSD (predicted vs. raw probabilities:  $r=0.976$ ). Adding respondents' female gender, lower education, and exposure to prior interpersonal trauma to the model yielded higher PTSD likelihood estimates, with similar model accuracy (predicted vs. raw probabilities:  $r=0.941$ ). The current model could be adjusted for other traumatic circumstances and accommodate risk factors not captured by the ICPP (e.g., biological, social). In line with their use in general medicine, risk estimate models can inform clinical choices in psychiatry. It is hoped that quantifying individuals' PTSD risk will be a first step towards systematic prevention of the disorder.*

**Key words:** Post-traumatic stress disorder, prediction, risk assessment tool, trauma survivors, clinician-administered PTSD scale for DSM-IV (CAPS), female gender, lower education, exposure to prior interpersonal trauma, prevention

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Post-traumatic stress disorder (PTSD) is the most frequent psychopathological consequence of traumatic events<sup>1,2</sup>. Chronic PTSD is tenacious, debilitating and frequently intractable<sup>3-9</sup>. Early PTSD symptoms are sensitive but non-specific predictors of chronic PTSD<sup>10</sup>. They subside in over 70% of those expressing them<sup>11-13</sup>, whilst few initially asymptomatic survivors develop delayed-onset PTSD<sup>14</sup>.

Early cognitive behavioral interventions significantly reduce the prevalence of PTSD, and their effect is stable<sup>8,15,16</sup>. These interventions, however, are resource-demanding, and unnecessary for low-risk survivors, whose symptoms subside spontaneously<sup>15,17</sup>. Thus, an accurate individual estimate of survivors' risk for chronic PTSD is a prerequisite for efficient prevention and service planning<sup>18</sup>.

Previous studies have had difficulty producing such estimates, due to the multiplicity, complexity and distributional variation of PTSD risk indicators. Additionally, most studies have attempted to predict cases (i.e., who will develop PTSD) rather than produce PTSD likelihood estimates for every participant (i.e., how likely is a person to develop PTSD)<sup>19,20</sup>.

Longitudinal studies have nonetheless reported numerous group-level PTSD risk indicators<sup>21,22</sup>, such as female gen-

der<sup>23,24</sup>, age<sup>23</sup>, education<sup>25</sup>, ethnicity<sup>26</sup>, lifetime exposure to traumatic events<sup>27</sup>, and marital status<sup>24</sup>. Several symptom-based case predictions have been developed, consistently performing better than chance<sup>28-31</sup>, but unable to build a reliable, personalized risk estimator<sup>32</sup>. Meta-analyses<sup>21,22</sup> and systematic reviews<sup>21,22,33,34</sup> have similarly endorsed group-level risk indicators without a clear path to clinical implementation<sup>34</sup>.

Trauma admissions to acute care centers and emergency departments (EDs) offer a first point of contact with numerous survivors at risk. EDs evaluate in the US over 39 million individuals yearly for treatment of traumatic injury<sup>35-39</sup>. Worldwide, road traffic accidents, a mainstay cause of ED admissions, cause an estimated 1.25 million deaths and over 20 million non-fatal injuries yearly<sup>40</sup>.

The prevalence of PTSD after ED admissions resembles that seen in survivors who do not require or receive ED care – e.g., 52% incidence of new PTSD among women survivors of interpersonal violence admitted to EDs vs. 51-76% among women surveyed in shelters, domestic-violence clinics and therapy groups<sup>41,42</sup>. The 18-month prevalence of PTSD among drivers admitted to general hospitals after injury-producing car crashes (11%) is somewhat higher than that of car drivers not seen in EDs (7%)<sup>43</sup>.

Quantifying individuals' PTSD risk following acute care trauma admission could provide an empirical foundation for mitigating and preventing a major public health issue. Towards that goal, members of the International Consortium to Predict PTSD (ICPP) shared item-level data from ten longitudinal, acute care based studies of the early development of PTSD, performed in the US, Australia, Japan, Israel, Switzerland, and The Netherlands. The data were harmonized, pooled into a single individual participant-level dataset (IPD) and submitted to data analysis.

An analysis of IPD, or mega-analysis, offers a sensible approach to aggregating data across studies<sup>44,45</sup>. Unlike systematic reviews and meta-analyses, mega-analyses do not rely on the original studies' data analytic approaches and reporting perspectives and enable direct estimates of parameters of interest (i.e., predictors, outcomes). This allows data source heterogeneity and subgroup variations to be examined directly, and makes it possible to interrogate the combined data in ways not considered, or impossible, in the component studies, due to their sample sizes or limited population diversity<sup>46,47</sup>.

In line with current medical risk assessment practices (e.g., in oncology<sup>48-50</sup>, surgery or cardiology<sup>51-54</sup>), we used the ICPP IPD to develop a prediction function that estimates the probability of PTSD given a set of early, observable risk indicators. Following replicated demonstrations of their predictive yield in classification models<sup>55-62</sup>, we positioned PTSD symptoms as a key predictor, subsequently enriching the predictive models by including other previously documented and clinically-obtainable risk indicators available in the ICPP dataset (e.g., gender, trauma type, lifetime trauma history).

## METHODS

### Studies, participants and variables

Using a previously described literature search strategy<sup>63</sup>, the ICPP IPD consisted of thirteen longitudinal acute-care based studies of recent trauma survivors conducted in six countries. Investigators obtained informed consent using procedures approved by their local institutional review boards. Item-level data from studies were shared, harmonized (see below) and combined into a pooled dataset. All ICPP studies used the DSM-IV PTSD template to infer PTSD diagnosis and symptom severity. Included in this report are the ten studies<sup>15,64-72</sup> that used the repeatedly validated Clinician-Administered PTSD Scale for DSM-IV (CAPS)<sup>73,74</sup>.

Study participants were included if they had an initial CAPS interview within 60 days of the traumatic event, and at least one follow-up CAPS assessment 4 to 15 months (122 to 456 days) after trauma exposure. These criteria were met by 2,473 participants (Table 1). To maximize the utility of prediction, we used the earliest observation for individuals with two early (<60 days) assessments, and the latest observation for those with multiple assessments during follow-up.

### PTSD severity and diagnosis

The CAPS quantifies the frequency and severity of each of the seventeen DSM-IV PTSD symptom criteria<sup>73</sup> by assigning to each symptom a 0-4 incremental frequency score and a 0-4 intensity score. A continuous measure of PTSD severity is obtained by adding all individual symptom scores (CAPS total score). A diagnosis of PTSD is determined using DSM-IV PTSD diagnostic criteria of at least one re-experiencing (Criterion B), three avoidance/numbing (Criterion C), and two hyperarousal (Criterion D) symptoms<sup>73</sup>. Following recommendations, a PTSD symptom was deemed "present" if its frequency score was 1 or more, and its intensity score was 2 or more<sup>74,75</sup>.

Information on DSM-IV Criterion E (duration of at least one month) and F (clinically significant distress or impairment) were collected in four out of the ten studies. A sensitivity analysis within these studies found very high concordance between diagnoses determined by meeting DSM-IV symptom criteria alone (i.e., criteria B through D) and those obtained using both the symptom criteria and the E and F criteria (sensitivity 0.92, specificity 1.00, Cohen's kappa=0.95). We consequently assumed PTSD diagnosis as present, across studies, based on meeting DSM-IV PTSD symptom criteria alone.

### Risk indicators

The study's primary risk indicator was PTSD severity at the initial assessment (CAPS<sub>0</sub>, range 0-136), with age, gender, ethnicity, educational attainment, lifetime history of trauma exposure, and current trauma type considered as additional predictors.

Differences in data collection and instruments across studies required harmonization of four risk indicators. Educational attainment, which varied by participating countries' schooling systems, was recoded into a binary variable of less than secondary education versus completion of at least secondary education. Recoding participants' lifetime exposure to traumatic events followed a previous demonstration of a strong association between interpersonal trauma and PTSD<sup>76</sup> and included: a) exposure to at least one instance of interpersonal violence (e.g., physical or sexual violence, war or terror), b) in the absence of the former, exposure to at least one instance of non-interpersonal trauma (e.g., road traffic accidents), and c) no trauma exposure. Traumatic events leading to current acute care admission were categorized as motor vehicle accidents, other non-interpersonal events, and interpersonal violence (e.g., assaults).

### Data completeness and handling missing observations

CAPS<sub>0</sub> data were available for all 2,473 participants. Data on age, gender, and current trauma were available for >99% of the sample. Marital status was missing in 4.5%, education in 6.2%, ethnicity in 12.3%, and prior trauma in 16.8% of the sample.

**Table 1** Key participant characteristics in contributing studies and in the total sample

	Hepp et al <sup>64</sup>	Shalev et al <sup>65</sup>	Jenewein et al <sup>67</sup>	Irish et al <sup>68</sup>	Bryant et al <sup>69</sup>	Shalev et al <sup>70</sup>	Shalev et al <sup>15</sup>	Matsuoka et al <sup>71</sup>	Mouthaan et al <sup>72</sup>	Frijling et al <sup>66</sup>	Total sample
Country	SUI	ISR	SUI	US	AUS	ISR	ISR	JPN	NLD	NLD	
Eligible participants (N)	109	27	255	143	825	103	529	92	348	42	2,473
Age (mean±SD)	38.0±13.1	28.4±10.5	41.3±12.9	39.1±15.4	38.7±13.6	31.9±11.7	37.2±12.0	38.8±16.1	44.5±15.7	36.9±14.0	39.0±13.9
Gender (% male)	74	59	67	53	72	60	51	66	61	50	63
High school education (%)	85	NA	83	93	68	90	81	83	78	64	77
Trauma type (%)											
Motor vehicle accident	60	85	31	100	65	82	82	100	65	69	69
Other non-interpersonal	40	7	69	0	29	5	6	0	32	21	25
Interpersonal	0	7	0	0	6	11	12	0	3	10	6
Prior trauma (%)											
None	NA	7	NA	48	27	42	33	45	41	50	29
Non-interpersonal	NA	67	NA	42	61	38	32	28	46	50	40
Interpersonal	NA	22	NA	7	12	19	27	27	13	0	14
Baseline CAPS score (mean±SD)	21.6±15.3	33.8±31.5	13.3±13.0	24.8±22.6	16.9±15.6	25.9±24.7	57.1±24.9	20.0±17.4	20.7±18.5	38.5±19.4	27.4±25.1
Endpoint PTSD (%)	3.7	25.9	4.3	9.1	9.9	19.4	23.6	8.7	5.7	2.4	11.8

CAPS – Clinician-Administered PTSD Scale for DSM-IV, PTSD – post-traumatic stress disorder, SUI – Switzerland, ISR – Israel, US – United States, AUS – Australia, JPN – Japan, NLD – The Netherlands, NA – not available

**Table 2** Comparison of participants with complete and incomplete data

Variable	Complete (N=1,682)	Incomplete (N=791)	p
Age (mean±SD)	37.5±14.1	39.0±13.6	0.347
CAPS <sub>0</sub> (mean±SD)	21.0±26.0	14.0±22.3	<0.001
Gender, N (%)			
Male	1,028 (66)	533 (34)	<0.001
Female	654 (72)	251 (28)	
Ethnicity, N (%)			
White	1,502 (76)	481 (24)	<0.001
Non-White	180 (97)	5 (3)	
Education, N (%)			
At least secondary education	1,389 (73)	505 (27)	0.057
Less than secondary education	293 (69)	133 (31)	
Marital status, N (%)			
Married/living with a partner	860 (74)	304 (26)	0.005
Single/not living with a partner	822 (69)	375 (31)	
Trauma type, N (%)			
Motor vehicle accident	1,285 (75)	421 (25)	<0.001
Other non-interpersonal	291 (47)	329 (53)	
Interpersonal	106 (77)	31 (23)	
Prior trauma, N (%)			
None	298 (86)	49 (14)	<0.001
Non-interpersonal	626 (87)	93 (13)	
Interpersonal	758 (76)	233 (24)	
Endpoint PTSD, N (%)			
No	1,474 (68)	708 (32)	0.178
Yes	208 (71)	83 (29)	

PTSD – post-traumatic stress disorder, CAPS<sub>0</sub> – baseline score on Clinician-Administered PTSD Scale for DSM-IV

Participants missing at least one variable (N=791; 32%) differed from those with complete data (N=1,682) with respect to several risk indicators (Table 2). To address these missing observations, we present analyses in which missing predictors were handled by multiple imputation using chained equations (MICE) performed on the IPD<sup>77</sup>. Ten imputed datasets were created after twenty iterations and the results were pooled using Rubin's method<sup>78</sup>. For completeness, we also computed the results using individuals who had complete data (i.e., without imputation). The results did not differ substantially from those obtained after imputation and are available upon request.

## Data analyses

Differences in frequency and severity of risk predictors between participants with and without endpoint PTSD were

assessed using Mann-Whitney tests for continuous risk predictors and  $\chi^2$  tests for categorical risk predictors. The number of participants endorsing each CAPS<sub>0</sub> severity score (smoothed for five-points intervals) was visualized using a histogram, separately for all participants and for those with PTSD at the study's endpoint.

The relatively large sample size in the ICPP dataset enabled us to obtain simple raw estimates of the probability of downstream PTSD for each CAPS<sub>0</sub> score. The estimator used was the fraction of PTSD cases among all individuals with a given CAPS<sub>0</sub> score, smoothed with a window of five adjacent points.

Logistic regression models were obtained using CAPS<sub>0</sub> as the only predictor (CAPS<sub>0</sub> model), CAPS<sub>0</sub> plus all risk predictors (full model), and CAPS<sub>0</sub> plus significant predictors only (significant predictors model). The models' fits were evaluated using the Brier score<sup>79</sup>, Efron's  $R^2$ , model's predicted-to-raw ratio, and the area under the receiver operating characteristic curve (AUC).

The Brier score<sup>79</sup> measures the accuracy of probabilistic predictions. It expresses the mean standard error of the squared difference between the estimated probabilities and the true PTSD classification. Its range is 0 to 1. A Brier score of zero represents a perfect model and scores of 0.25 or greater signal a non-informative model. Efron's  $R^2$  is the correlation between the predicted probabilities and the smoothed probabilities.

Two options were considered for selecting the regression model's intercept: a fixed effects intercept, where a common intercept is estimated after pooling or "stacking" the data together, and a random effects intercept, where the intercept is allowed to vary by study<sup>44</sup>. Random effects (or stratified approaches) have not been recommended when the prevalence of an outcome varies substantially between studies<sup>44</sup>, as is the case with the ICPP studies. Alternatively, it could be hypothesized that heterogeneity in endpoint PTSD prevalence across ICPP studies reflected heterogeneity in the distribution of CAPS<sub>0</sub> severity across studies, which was due to variability in studies' sampling routine. Under this hypothesis, ICPP studies could be seen as representing different samplings from a common parent population of acute care trauma admissions.

To evaluate the two models, we compared the predictive fits of the fixed effects and the random effects logistic regressions with CAPS<sub>0</sub> as the only predictor, using a bootstrap approach where participants were randomly sampled with replacement, models were obtained, and then predicted probabilities from both models were estimated among the left-out participants. For each approach, the ratio of expected PTSD diagnoses and actual PTSD diagnoses (expected/observed or E/O), the calibration slope  $\beta_{\text{overall}}$  (the slope from a logistic regression of the predicted probabilities on endpoint PTSD), and the Brier score were obtained. An E/O far from 1 indicates whether the model's intercept, which determines the predicted prevalence of PTSD, is too high or too low, while the calibration slope reflects heterogeneity of the predictor-outcome associations or over-fitting of the data<sup>44</sup>. This process was repeated 100 times with statistics averaged across iterations. A finding of poorer results in the



fixed effects model compared to the random effects model would indicate that the studies were too heterogeneous to be analyzed together after accounting for differences in the distribution of CAPS<sub>0</sub>.

Differences in the predicted probability of PTSD given different risk factors were estimated by drawing 1,000 posterior simulations of each model's  $\beta$  coefficients, predicting endpoint PTSD at each value of CAPS<sub>0</sub> with different risk profiles (e.g., male versus female gender), and evaluating the differences in the predicted probabilities across baseline CAPS<sub>0</sub> scores<sup>80</sup>.

The selected time window for determining endpoint PTSD status (122-456 days; 4-15 months) maximized the number of ICPP studies included in each time interval. To evaluate whether the substantial width of that time window affected the

results, and to additionally produce an estimate of prolonged PTSD likelihood, we repeated the logistic regressions using participants whose PTSD status was obtained 9 to 15 months (273-456 days) after the traumatic events.

## RESULTS

### Participants' characteristics, risk predictors, and CAPS<sub>0</sub> scores

Participants' average age at studies' onset was 39.0±13.9 years. There were fewer female participants (37%) in the sample than males. Motor vehicle accidents (69%) were the most common in-

**Table 3** Sample variables stratified by endpoint post-traumatic stress disorder (PTSD) status

Variable	No endpoint PTSD	Endpoint PTSD	Total sample	p
N (%)	2,182 (88)	291 (12)	2,473	
Age (mean±SD)	38.0±14.2	39.0±11.8	39.0±13.9	0.366
CAPS <sub>0</sub> (mean±SD)	23.1±21.4	59.6±27.8	27.4±25.1	<0.001
Gender, N (%)				
Male	1,418 (91)	143 (9)	1,561	<0.001
Female	757 (84)	148 (16)	905	
Missing			7 (0.3)	
Ethnicity, N (%)				
White	1,742 (88)	241 (12)	1,983	0.592
Non-White	165 (89)	20 (11)	185	
Missing			305 (12.3)	
Education, N (%)				
At least secondary education	1,698 (90)	196 (10)	1,894	0.051
Less than secondary education	368 (86)	58 (14)	426	
Missing			153 (6.2)	
Marital status, N (%)				
Married/living with a partner	1,035 (89)	129 (11)	1,164	0.780
Single/not living with a partner	1,060 (89)	137 (11)	1,197	
Missing			112 (4.5)	
Current trauma type, N (%)				
Motor vehicle accident	1,485 (87)	221 (13)	1,706	<0.001
Other non-interpersonal	588 (95)	32 (5)	620	
Interpersonal	100 (73)	37 (27)	137	
Missing			10 (0.4)	
Prior trauma, N (%)				
None	308 (89)	39 (11)	347	0.061
Non-interpersonal	641 (89)	78 (11)	719	
Interpersonal	848 (86)	143 (14)	991	
Missing			416 (16.8)	

Comparisons (p values) are between participants with vs. without endpoint PTSD  
CAPS<sub>0</sub> – baseline score on Clinician-Administered PTSD Scale for DSM-IV

dex trauma, followed by other types of non-interpersonal trauma (25%) and interpersonal trauma (6%). The median time to the initial assessment was 15±16.7 days (range 1-60). The median time to the endpoint assessment was 333±103.1 days (range 122-456).

The prevalence of endpoint PTSD was 11.8% (N=291). Endpoint PTSD was significantly more frequent among female participants (16.4%, compared to 9.2% in males,  $p<0.001$ ) and among participants who suffered interpersonal trauma compared to a motor vehicle accident or other traumatic events (respectively, 27%, 5% and 13%,  $p<0.001$ ). No significant differences were observed by ethnicity, marital status, or age (see Table 3).

The histogram in Figure 1 displays the number of participants who endorsed each CAPS<sub>0</sub> score, smoothed for a five points interval. As can be seen, the total number of participants declines progressively with increasing CAPS<sub>0</sub> scores. The CAPS<sub>0</sub> scores of participants with endpoint PTSD, however, span across the instrument's severity range, such that the proportion of those with endpoint PTSD increases with increasing CAPS<sub>0</sub> severity.

## Prediction of endpoint PTSD

The results from fixed effect models using CAPS<sub>0</sub> alone (CAPS<sub>0</sub> model), CAPS<sub>0</sub> plus all available predictors (full model), and CAPS<sub>0</sub> plus significant predictors only (significant predictors model) are presented in Table 4.

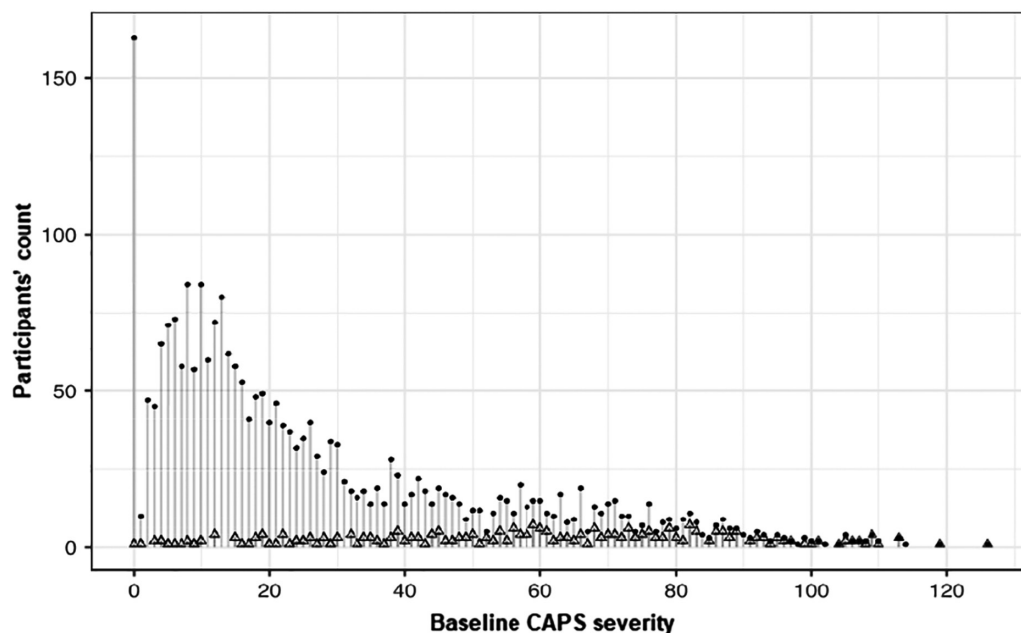
The CAPS<sub>0</sub> model (plotted in Figure 2 along with its 95% confidence interval) fits well (Efron's  $R^2=0.230$ , Brier score=0.080, AUC=0.847), with a very high correlation between the model's

predicted probability and the smoothed estimate of conditional probability ( $r=0.976$ ). Logistic regression using the full model showed that female gender ( $\beta=0.309$ ,  $SE=0.151$ ,  $p=0.041$ ), having less than a secondary education ( $\beta=0.486$ ,  $SE=0.188$ ,  $p=0.009$ ), and prior interpersonal trauma ( $\beta=0.662$ ,  $SE=0.238$ ,  $p=0.006$ ) contributed significantly to the PTSD outcome.

With the inclusion of all risk indicators (full model) or that of significantly contributing factors (significant predictors model), accuracy remained high (respectively, smoothed probability correlation=0.941, Efron's  $R^2=0.246$ , Brier score=0.078, AUC=0.855; and smoothed probability correlation=0.946, Efron's  $R^2=0.246$ , Brier score=0.078, AUC=0.851). Thus, the addition of female gender, lifetime exposure to interpersonal violence, and less than a secondary education to the CAPS<sub>0</sub> model increased PTSD likelihood whilst keeping the CAPS<sub>0</sub> model's accuracy.

In the bootstrap analysis comparing the fixed effects logistic model with a random effects model using only CAPS<sub>0</sub> as a predictor, the E/O ratio and  $\beta_{\text{overall}}$  from the fixed effects model (1.01 and 1.00, respectively) were closer to 1.00 than the random effects model (1.14 and 0.75, respectively), and the Brier score was lower on average for the fixed effects model (0.081, SD=0.01) than the random effects model (0.084, SD=0.01). Overall, the fixed effects model seems to estimate the likely number of participants with PTSD at follow-up more accurately, with less heterogeneity or over-fitting, than the random effects model, thereby supporting the pooling of participating studies.

After accounting for the CAPS<sub>0</sub> effect, female participants were found to have a maximum of 5% (95% CI: -2% to 12%) higher risk for endpoint PTSD compared to male participants. Moreover, participants with all significant risk factors (i.e.,



**Figure 1** Histogram of participants' baseline PTSD symptoms severity scores (CAPS<sub>0</sub> total scores). Dots represent individual participants; overlaid triangles those who subsequently developed PTSD. PTSD – post-traumatic stress disorder, CAPS<sub>0</sub> – baseline score on Clinician-Administered PTSD Scale for DSM-IV.



**Table 4** Coefficients (with SE) and fit statistics from the CAPS<sub>0</sub>, significant predictors and full models

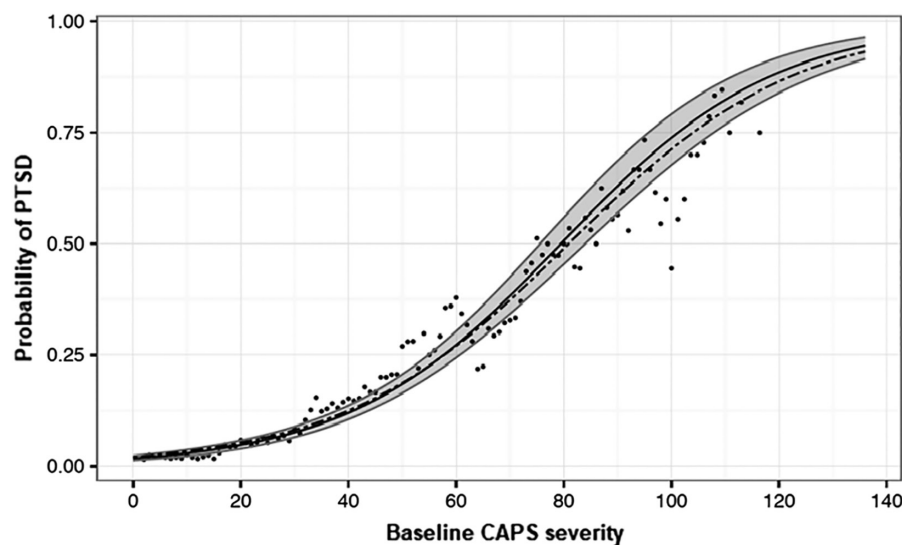
Model parameters	CAPS <sub>0</sub> model	Significant predictors model	Full model
Intercept	−3.981*** (0.149)	−4.628*** (0.27)	−4.659*** (0.377)
CAPS <sub>0</sub>	0.05*** (0.003)	0.051*** (0.003)	0.05*** (0.003)
Female	-	0.307* (0.149)	0.309* (0.151)
Age	-	-	0 (0.006)
Less than secondary education	-	0.483** (0.186)	0.486** (0.188)
Non-White	-	-	0.42 (0.281)
Single	-	-	0.051 (0.164)
Current traumatic event			
Interpersonal	-	-	0.286 (0.255)
Other	-	-	−0.201 (0.222)
Lifetime trauma exposure			
Non-interpersonal	-	0.113 (0.249)	0.128 (0.249)
Interpersonal	-	0.656** (0.237)	0.662** (0.238)
Efron's R <sup>2</sup>	0.23	0.246	0.246
Smoothed probability correlation	0.976	0.946	0.941
Brier score	0.08	0.078	0.078
AUC	0.847	0.851	0.855

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

CAPS<sub>0</sub> – baseline score on Clinician-Administered PTSD Scale for DSM-IV, AUC – area under receiver operating characteristic curve

female gender, less than secondary education, and exposure to prior interpersonal trauma) had a 34% (95% CI: 20-48%) higher risk of PTSD compared to participants without any significant risk factors (i.e., male with secondary education

and no prior interpersonal trauma). Estimated probabilities and 95% confidence intervals for endpoint PTSD based on each combination of the significant predictors are provided in Table 5.



**Figure 2** Predicted probabilities of endpoint PTSD conditional on initial (CAPS<sub>0</sub>) severity scores. The dots represent the raw conditional probability of PTSD at follow-up given the CAPS<sub>0</sub> score, smoothed with a kernel of width 5. The solid black line represents the logistic model predicted probability given the CAPS<sub>0</sub> score. The gray area is the 95% confidence interval for the prediction model. The dashed line represents the prediction function derived from participants with follow-up observations later than 9 months. PTSD – post-traumatic stress disorder, CAPS<sub>0</sub> – baseline score on Clinician-Administered PTSD Scale for DSM-IV.

**Table 5** Estimated probabilities (with 95% CIs) of endpoint PTSD diagnosis by incremental values of CAPS<sub>0</sub> scores

CAPS <sub>0</sub> total score	Probability of PTSD (CAPS <sub>0</sub> alone)	Probability of PTSD by gender (CAPS <sub>0</sub> plus gender)		Probability of PTSD by gender (CAPS <sub>0</sub> , plus less than secondary education, and prior interpersonal trauma)	
		Males	Females	Males	Females
0	0.018 (0.014-0.024)	0.017 (0.013-0.023)	0.021 (0.015-0.029)	0.030 (0.020-0.043)	0.041 (0.025-0.061)
5	0.024 (0.018-0.030)	0.022 (0.017-0.029)	0.027 (0.020-0.037)	0.038 (0.026-0.054)	0.052 (0.033-0.076)
10	0.03- (0.024-0.038)	0.028 (0.021-0.036)	0.034 (0.025-0.046)	0.049 (0.034-0.068)	0.065 (0.042-0.095)
15	0.038 (0.031-0.047)	0.035 (0.028-0.045)	0.043 (0.033-0.056)	0.062 (0.044-0.085)	0.083 (0.054-0.119)
20	0.048 (0.040-0.059)	0.045 (0.036-0.056)	0.055 (0.042-0.070)	0.079 (0.056-0.106)	0.104 (0.070-0.147)
25	0.061 (0.051-0.073)	0.057 (0.046-0.069)	0.069 (0.054-0.086)	0.099 (0.071-0.132)	0.130 (0.089-0.181)
30	0.077 (0.066-0.090)	0.071 (0.059-0.086)	0.086 (0.069-0.106)	0.124 (0.091-0.163)	0.161 (0.113-0.220)
35	0.097 (0.084-0.112)	0.090 (0.075-0.106)	0.108 (0.088-0.130)	0.154 (0.114-0.201)	0.198 (0.142-0.265)
40	0.121 (0.106-0.138)	0.112 (0.094-0.132)	0.134 (0.111-0.161)	0.190 (0.143-0.245)	0.241 (0.177-0.317)
45	0.150 (0.133-0.169)	0.139 (0.117-0.162)	0.165 (0.139-0.195)	0.232 (0.177-0.296)	0.290 (0.218-0.375)
50	0.185 (0.165-0.207)	0.171 (0.145-0.199)	0.202 (0.172-0.235)	0.280 (0.217-0.352)	0.345 (0.264-0.436)
55	0.226 (0.201-0.251)	0.208 (0.176-0.241)	0.244 (0.209-0.284)	0.334 (0.262-0.413)	0.404 (0.315-0.500)
60	0.272 (0.243-0.302)	0.252 (0.213-0.292)	0.293 (0.253-0.337)	0.392 (0.312-0.477)	0.466 (0.372-0.564)
65	0.324 (0.289-0.360)	0.301 (0.256-0.349)	0.346 (0.300-0.393)	0.453 (0.367-0.543)	0.528 (0.431-0.626)
70	0.381 (0.340-0.423)	0.355 (0.302-0.410)	0.404 (0.352-0.455)	0.516 (0.425-0.608)	0.590 (0.492-0.685)
75	0.442 (0.394-0.488)	0.413 (0.353-0.475)	0.464 (0.406-0.519)	0.579 (0.484-0.670)	0.649 (0.553-0.739)
80	0.504 (0.450-0.555)	0.474 (0.409-0.540)	0.525 (0.463-0.582)	0.638 (0.544-0.726)	0.704 (0.612-0.787)
85	0.566 (0.507-0.621)	0.535 (0.465-0.604)	0.586 (0.519-0.644)	0.694 (0.602-0.776)	0.754 (0.668-0.829)
90	0.625 (0.564-0.682)	0.595 (0.524-0.665)	0.644 (0.576-0.702)	0.745 (0.657-0.819)	0.797 (0.720-0.864)
95	0.682 (0.619-0.738)	0.653 (0.579-0.722)	0.698 (0.631-0.752)	0.790 (0.708-0.855)	0.835 (0.765-0.893)
100	0.733 (0.671-0.787)	0.706 (0.632-0.772)	0.747 (0.682-0.798)	0.828 (0.754-0.886)	0.867 (0.805-0.916)
105	0.778 (0.719-0.830)	0.754 (0.682-0.816)	0.790 (0.729-0.838)	0.861 (0.795-0.911)	0.893 (0.840-0.934)
110	0.818 (0.763-0.864)	0.796 (0.730-0.853)	0.828 (0.769-0.871)	0.888 (0.830-0.931)	0.915 (0.869-0.949)
115	0.852 (0.801-0.893)	0.833 (0.773-0.883)	0.860 (0.807-0.899)	0.911 (0.861-0.946)	0.932 (0.894-0.961)
120	0.881 (0.835-0.917)	0.864 (0.809-0.909)	0.887 (0.839-0.921)	0.929 (0.887-0.959)	0.947 (0.915-0.970)
125	0.904 (0.864-0.935)	0.890 (0.840-0.929)	0.909 (0.867-0.938)	0.944 (0.908-0.968)	0.958 (0.931-0.977)
130	0.924 (0.888-0.950)	0.912 (0.868-0.945)	0.927 (0.890-0.952)	0.956 (0.926-0.976)	0.967 (0.945-0.982)
135	0.939 (0.909-0.962)	0.929 (0.892-0.957)	0.942 (0.910-0.963)	0.965 (0.940-0.981)	0.974 (0.956-0.986)

PTSD – post-traumatic stress disorder, CAPS<sub>0</sub> – baseline score on Clinician-Administered PTSD Scale for DSM-IV. For the full array of risk indicator combinations, see [https://wvdmci.shinyapps.io/PTSD\\_Risk\\_Lookup/](https://wvdmci.shinyapps.io/PTSD_Risk_Lookup/).

Using data from participants whose last follow-up assessment fell between 9 and 15 months from the traumatic event (N=1,359) to fit a CAPS<sub>0</sub>-only logistic regression yielded similar prediction probabilities (see dotted line in Figure 2), with similar model accuracy (Efron's R<sup>2</sup>=0.195, Brier score=0.071, AUC=0.822).

## DISCUSSION

The results of this study demonstrate that the probability of meeting PTSD diagnostic criteria 4 to 15 months after acute care admission is reliably modeled by a logistic function of

initial PTSD symptom severity. Added to this model, female gender, having less than secondary education, and prior interpersonal trauma were associated with higher likelihood of endpoint PTSD. Other previously documented risk factors, such as age, marital status, and current trauma type, did not improve the prediction over the model that had CAPS<sub>0</sub> score as the only predictor. Importantly, the limited margin of error of the resulting risk estimate enables its clinical use to assess PTSD likelihood for each combination of the significant risk indicators.

The limited incremental effect of several known risk factors was an unexpected finding, suggesting that the contribution of

these factors to PTSD likelihood is mediated by their effect on early symptom severity. In line with this view, a previous comparison of PTSD following terror attacks with PTSD following motor vehicle accidents from the same ED has shown that the higher prevalence of 4-month PTSD following terror attacks (38% vs. 19%) was entirely accounted for by survivors' early responses, that included one-week PTSD symptoms, ED heart rate and peri-traumatic dissociation<sup>61</sup>.

Our results extend previous findings of an association between high initial PTSD symptoms and being diagnosed with PTSD<sup>55-62</sup> by highlighting the added informational value of likelihood estimates relative to predictive classification. The uniform distribution of PTSD participants initial CAPS<sub>0</sub> scores illustrates a barrier to classification models: trauma survivors who ultimately developed PTSD had their initial symptom severity distributed across the entire range of CAPS<sub>0</sub> total scores, thereby defying the use of a threshold separating future cases from non-cases. Predicting who will develop PTSD, as much as predicting who among heavy smokers will develop lung cancer, is a difficult task, frequently replaced by likelihood estimates. Classification models have significantly informed our understanding of disorders' etiology and pathogenesis<sup>81-86</sup>. Likelihood estimates, however, may be better suited for quantifying individual risk. As in other areas of medicine<sup>48-54</sup>, quantifying risk ultimately informs clinical action.

How can our results inform clinical action? Consider, for example, three female survivors with a CAPS<sub>0</sub> score of, respectively, 20, 40, 60; less than secondary education, and lifetime exposure to interpersonal violence. These individuals will have, respectively, 10.4% (95% CI: 7.0-14.7), 24.1% (95% CI: 17.7-31.7) and 46.6% (95% CI: 37.2-56.4) likelihood of chronic PTSD. Male survivors with the same initial scores and no additional risk factors will have, respectively, 2.7% (95% CI: 1.8-4.0), 7.1% (95% CI: 4.8-10.1) and 17.3% (95% CI: 12.2-23.4) likelihood of chronic PTSD. Individuals endorsing the highest CAPS<sub>0</sub> score, in both genders, might be seen as requiring clinical attention, e.g., an early intervention. The lower scores may justify a "watchful wait" with additional assessments.

A strength of this study follows from the use of data on a large number of participants from culturally and geographically diverse settings. Each included investigation utilized a longitudinal design, assessed PTSD symptoms shortly after index trauma, and based its appraisal of symptoms and diagnostic status on the repeatedly validated CAPS instrument.

In interpreting our findings, one should nonetheless consider some limitations. First, the time frame to determine PTSD status in our main analyses was 4-15 months, thus very wide. However, when the data were restricted to participants re-interviewed more than 9 months after the trauma, the resulting logistic prediction model remained essentially unchanged. Our prediction is nonetheless calibrated for the wider and earlier time bracket and centered on 333.0±103.1 days (less than a year) from trauma exposure.

Second, several risk predictors were harmonized due to the variety of instruments used by site investigators, which resulted

in a loss of granularity. While those harmonized variables (less than secondary education, lifetime interpersonal trauma) have contributed to PTSD probability estimates, results involving recoded variables may miss important predictors' information. Simplified predictors, however, might be easier to obtain in clinical practice and are widely used in predictive models in other areas of medicine (e.g., "smoking yes/no" and "diabetes yes/no" in the Framingham 10 years cardiovascular disease risk score).

Third, the ICPP data display considerable heterogeneity among contributing studies, which, as discussed above, raised methodological concerns about the best approach to pooling the data. We found that the fixed effects model was more accurate than the data source dependent random effects model and thus justified pooling from different studies. We also believe that a fixed effects model is more applicable to new environments, because a global slope and intercept were estimated across studies. Our choice, however, is neither beyond critique nor without significance: large multi-source data compilations are currently evaluated in genetic, genomic and imaging research<sup>87</sup>, all of which have to contend with data source heterogeneity resembling the ICPP effort. Our theoretical premise that ICPP studies were differentially sampling subsets of an underlying population of reference (i.e., acute care trauma admissions) should be corroborated by testing the resulting risk assessment tool in newly admitted acute care trauma survivors.

The use of the CAPS structured clinical interview may add some burden on service delivery, and that interview is not properly a screening instrument. Moreover, several PTSD (i.e., CAPS) symptoms (e.g., insomnia, avoidance, inability to recall important aspects of the traumatic event) may not be present during ED admission. The early CAPS, nonetheless, is a robust risk indicator. Future work should explore earlier and simpler screening alternatives, or establish stepwise "screening and prediction" models, starting upon ED admission and predicting the likelihood of expressing high levels of early PTSD symptoms.

Finally, our model was developed using acute care trauma admissions, and as such its implementation in other traumatic circumstances (e.g., prolonged adversities such as wars, captivity and relocation) may require adjustments. Notwithstanding the precise risk estimates for other traumatic circumstances, we believe that early symptom severity has been convincingly shown here to be a major predictor of PTSD risk, and that, as such, its evaluation among individual survivors provides a valid warning and a call for action.

These limitations do not take away from the robustness of our likelihood estimates and their ability to support a personal risk assessment in individual survivors. Similar risk estimate tools are used in other medical domains to support clinical decisions (e.g., for determining breast<sup>48</sup> or lung<sup>49,50</sup> cancer likelihood given risk indicators). The risk estimates provided in this work can be similarly used to trigger action (either watchful follow-up or early intervention) according to local resources and the desirability of prevention.

Quantifying individual risk is a step forward in planning services and interventions, better targeting high-risk individuals,

and ultimately decreasing the burden of PTSD following acute care admission.

## APPENDIX

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## REFERENCES

- Stein DJ, Karam EG, Shahly V et al. Post-traumatic stress disorder associated with life-threatening motor vehicle collisions in the WHO World Mental Health Surveys. *BMC Psychiatry* 2016;16:257.
- Hoge CW, Castro CA, Messer SC et al. Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *N Engl J Med* 2004;351:13-22.
- Kessler RC. Posttraumatic stress disorder: the burden to the individual and to society. *J Clin Psychiatry* 2000;61(Suppl. 5):4-12.
- Breslau N, Peterson E, Poisson L et al. Estimating post-traumatic stress disorder in the community: lifetime perspective and the impact of typical traumatic events. *Psychol Med* 2004;34:889-98.
- Committee on the Assessment of Ongoing Efforts in the Treatment of Post-traumatic Stress Disorder; Board on the Health of Select Populations; Institute of Medicine. Treatment for posttraumatic stress disorder in military and veteran populations: final assessment. Washington: Institute of Medicine National Research Council, 2014.
- Roberts NP, Roberts PA, Jones N et al. Psychological therapies for post-traumatic stress disorder and comorbid substance use disorder. *Cochrane Database Syst Rev* 2016;4:CD010204.
- Sijbrandij M, Kleiboer A, Bisson JI et al. Pharmacological prevention of post-traumatic stress disorder and acute stress disorder: a systematic review and meta-analysis. *Lancet Psychiatry* 2015;2:413-21.
- Roberts NP, Roberts PA, Jones N et al. Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: a systematic review and meta-analysis. *Clin Psychol Rev* 2015;38:25-38.
- Hoskins M, Pearce J, Bethell A et al. Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. *Br J Psychiatry* 2015;206:93-100.
- Andrews B, Brewin CR, Philpott R et al. Delayed-onset posttraumatic stress disorder: a systematic review of the evidence. *Am J Psychiatry* 2007;164:1319-26.
- Bryant RA, Nickerson A, Creamer M et al. Trajectory of post-traumatic stress following traumatic injury: 6-year follow-up. *Br J Psychiatry* 2015;206:417-23.
- Galatzer-Levy IR, Ankri Y, Freedman S et al. Early PTSD symptom trajectories: persistence, recovery, and response to treatment: results from the Jerusalem Trauma Outreach and Prevention Study (J-TOPS). *PLoS One* 2013;8:e70084.
- Kessler RC, Rose S, Koenen KC et al. How well can post-traumatic stress disorder be predicted from pre-trauma risk factors? An exploratory study in the WHO World Mental Health Surveys. *World Psychiatry* 2014;13:265-74.
- Smid GE, Moeren TT, van der Mast RC et al. Delayed posttraumatic stress disorder: systematic review, meta-analysis, and meta-regression analysis of prospective studies. *J Clin Psychiatry* 2009;70:1572-82.
- Shalev AY, Ankri Y, Israeli-Shalev Y et al. Prevention of posttraumatic stress disorder by early treatment: results from the Jerusalem Trauma Outreach and Prevention Study. *Arch Gen Psychiatry* 2012;69:166-76.
- Roberts NP, Kitchiner NJ, Kenardy J et al. Multiple session early psychological interventions for the prevention of post-traumatic stress disorder. *Cochrane Database Syst Rev* 2009;3:CD006869.
- Sijbrandij M, Olff M, Reitsma JB et al. Treatment of acute posttraumatic stress disorder with brief cognitive behavioral therapy: a randomized controlled trial. *Am J Psychiatry* 2007;164:82-90.
- Bryant RA. Early predictors of posttraumatic stress disorder. *Biol Psychiatry* 2003;53:789-95.
- Galatzer-Levy IR, Ma S, Statnikov A et al. Utilization of machine learning for prediction of post-traumatic stress: a re-examination of cortisol in the prediction and pathways to non-remitting PTSD. *Transl Psychiatry* 2017;7:e1070.
- Bryant RA, O'Donnell ML, Creamer M et al. A multisite analysis of the fluctuating course of posttraumatic stress disorder. *JAMA Psychiatry* 2013;70:839-46.
- Brewin CR, Andrews B, Valentine JD. Meta-analysis of risk factors for post-traumatic stress disorder in trauma-exposed adults. *J Consult Clin Psychol* 2000;68:748-66.
- Ozer EJ, Best SR, Lipsey TL et al. Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis. *Psychol Bull* 2003;129:52-73.
- Mollica RF, Sarajlic N, Chernoff M et al. Longitudinal study of psychiatric symptoms, disability, mortality, and emigration among Bosnian refugees. *JAMA* 2001;286:546-54.
- Silver RC, Holman EA, McIntosh DN et al. Nationwide longitudinal study of psychological responses to September 11. *JAMA* 2002;288:1235-44.
- Dougall AL, Ursano RJ, Posluszny DM et al. Predictors of posttraumatic stress among victims of motor vehicle accidents. *Psychosom Med* 2001;63:402-11.
- Koenen KC, Stellman JM, Stellman SD et al. Risk factors for course of post-traumatic stress disorder among Vietnam veterans: a 14-year follow-up of American legionnaires. *J Consult Clin Psychol* 2003;71:980-6.
- Ryb GE, Dischinger PC, Read KM et al. PTSD after severe vehicular crashes. *Ann Adv Automot Med* 2009;53:177-93.
- Ehring T, Kleim B, Clark DM et al. Screening for posttraumatic stress disorder: what combination of symptoms predicts best? *J Nerv Ment Dis* 2007;195:1004-12.
- Mouthaan J, Sijbrandij M, Reitsma JB et al. Comparing screening instruments to predict posttraumatic stress disorder. *PLoS One* 2014;9:e97183.
- Walters JT, Bisson JI, Shepherd JP. Predicting post-traumatic stress disorder: validation of the Trauma Screening Questionnaire in victims of assault. *Psychol Med* 2007;37:143-50.
- O'Donnell ML, Creamer MC, Parslow R et al. A predictive screening index for posttraumatic stress disorder and depression following traumatic injury. *J Consult Clin Psychol* 2008;76:923-32.
- Smits N, Smit F, Cuijpers P et al. Using decision theory to derive optimal cut-off scores of screening instruments: an illustration explicating costs and benefits of mental health screening. *Int J Methods Psychiatr Res* 2007;16:219-29.
- Brewin CR. Risk factor effect sizes in PTSD: what this means for intervention. *J Trauma Dissociation* 2005;6:123-30.
- Heron-Delaney M, Kenardy J, Charlton E et al. A systematic review of predictors of posttraumatic stress disorder (PTSD) for adult road traffic crash survivors. *Injury* 2013;44:1413-22.
- Kilpatrick DG, Resnick HS, Milanak ME et al. National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria. *J Trauma Stress* 2013;26:537-47.
- Bonnie RJ, Fulco CE, Liverman CT (eds). Reducing the burden of injury: advancing prevention and treatment. Washington: National Academy Press, 1999.
- LF MC. National hospital ambulatory medical care survey emergency department summary. Advance Data from Vital and Health Statistics, Vol. 245. Hyattsville: National Center for Health Statistics, 1992:1994.
- Rice DP, MacKenzie EJ, Jones AS et al. Cost of injury in the United States: a report to Congress. San Francisco: Institute for Health and Aging, University of California; Baltimore: Injury Prevention Center, Johns Hopkins University, 1989.
- Bergen GS, National Center for Health Statistics (U.S.). Injury in the United States: 2007 chartbook. Hyattsville: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2008.
- Ameratunga S, Hajar M, Norton R. Road-traffic injuries: confronting disparities to address a global-health problem. *Lancet* 2006;367:1533-40.
- Lipsky S, Field CA, Caetano R et al. Posttraumatic stress disorder symptomatology and comorbid depressive symptoms among abused women referred from emergency department care. *Violence Vict* 2005;20:645-59.



42. Golding JM. Intimate partner violence as a risk factor for mental disorders: a meta-analysis. *J Fam Violence* 1999;14:99-132.
43. Ameratunga S, Tin ST, Coverdale J et al. Posttraumatic stress among hospitalized and nonhospitalized survivors of serious car crashes: a population-based study. *Psychiatr Serv* 2009;60:402-4.
44. Debray T, Moons KG, Ahmed I et al. A framework for developing, implementing, and evaluating clinical prediction models in an individual participant data meta-analysis. *Stat Med* 2013;32:3158-80.
45. Chalmers I. The Cochrane collaboration: preparing, maintaining, and disseminating systematic reviews of the effects of health care. *Ann N Y Acad Sci* 1993;703:156-65.
46. Brincks A, Montag S, Howe GW et al. Addressing methodologic challenges and minimizing threats to validity in synthesizing findings from individual-level data across longitudinal randomized trials. *Prev Sci* 2018;19(Suppl. 1): 60-73.
47. Bainter SA, Curran PJ. Advantages of integrative data analysis for developmental research. *J Cogn Dev* 2015;16:1-10.
48. Gail MH, Brinton LA, Byar DP et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst* 1989;81:1879-86.
49. Cassidy A, Duffy SW, Myles JP et al. Lung cancer risk prediction: a tool for early detection. *Int J Cancer* 2007;120:1-6.
50. Cassidy A, Myles JP, van Tongeren M et al. The LLP risk model: an individual risk prediction model for lung cancer. *Br J Cancer* 2008;98:270-6.
51. Chan DXH, Sim YE, Chan YH et al. Development and validation of the Combined Assessment of Risk Encountered in Surgery (CARES) surgical risk calculator for prediction of postsurgical mortality and need for intensive care unit admission risk: a single-center retrospective study. *BMJ Open* 2018;8: e019427.
52. Cook NR, Ridker PM. Further insight into the cardiovascular risk calculator: the roles of statins, revascularizations, and underascertainment in the Women's Health Study. *JAMA Intern Med* 2014;174:1964-71.
53. Fox ER, Samdarshi TE, Musani SK et al. Development and validation of risk prediction models for cardiovascular events in black adults: the Jackson Heart Study Cohort. *JAMA Cardiol* 2016;1:15-25.
54. Hippisley-Cox J, Coupland C, Robson J et al. Derivation, validation, and evaluation of a new QRISK model to estimate lifetime risk of cardiovascular disease: cohort study using QResearch database. *BMJ* 2010;341:c6624.
55. Blanchard EB, Hickling EJ, Forneris CA et al. Prediction of remission of acute posttraumatic stress disorder in motor vehicle accident victims. *J Trauma Stress* 1997;10:215-34.
56. Frommberger UH, Stieglitz RD, Nyberg E et al. Prediction of posttraumatic stress disorder by immediate reactions to trauma: a prospective study in road traffic accident victims. *Eur Arch Psychiatry Clin Neurosci* 1998;248:316-21.
57. Jehel L, Paterniti S, Brunet A et al. Prediction of the occurrence and intensity of post-traumatic stress disorder in victims 32 months after bomb attack. *Eur Psychiatry* 2003;18:172-6.
58. Karstoft KI, Galatzer-Levy IR, Statnikov A et al. Bridging a translational gap: using machine learning to improve the prediction of PTSD. *BMC Psychiatry* 2015;15:30.
59. Matsuoka Y, Nishi D, Nakajima S et al. Incidence and prediction of psychiatric morbidity after a motor vehicle accident in Japan: the Tachikawa Cohort of Motor Vehicle Accident Study. *Crit Care Med* 2008;36:74-80.
60. Mayou R, Bryant A, Ehlers A. Prediction of psychological outcomes one year after a motor vehicle accident. *Am J Psychiatry* 2001;158:1231-8.
61. Shalev AY, Freedman S. PTSD following terrorist attacks: a prospective evaluation. *Am J Psychiatry* 2005;162:1188-91.
62. Shalev AY, Freedman S, Peri T et al. Predicting PTSD in trauma survivors: prospective evaluation of self-report and clinician-administered instruments. *Br J Psychiatry* 1997;170:558-64.
63. Qi W, Ratanatharathorn A, Gevonden M et al. Application of data pooling to longitudinal studies of early post-traumatic stress disorder (PTSD): the International Consortium to Predict PTSD (ICPP) project. *Eur J Psychotraumatol* 2018;9:1476442.
64. Hepp U, Moergeli H, Buchi S et al. Post-traumatic stress disorder in serious accidental injury: 3-year follow-up study. *Br J Psychiatry* 2008;192: 376-83.
65. Shalev AY, Peri T, Brandes D et al. Auditory startle response in trauma survivors with posttraumatic stress disorder: a prospective study. *Am J Psychiatry* 2000;157:255-61.
66. Frijling JL, van Zuiden M, Koch SBJ et al. Efficacy of oxytocin administration early after psychotrauma in preventing the development of PTSD: study protocol of a randomized controlled trial. *BMC Psychiatry* 2014;14:92.
67. Jenewein J, Wittmann L, Moergeli H et al. Mutual influence of posttraumatic stress disorder symptoms and chronic pain among injured accident survivors: a longitudinal study. *J Trauma Stress* 2009;22:540-8.
68. Irish L, Ostrowski SA, Fallon W et al. Trauma history characteristics and subsequent PTSD symptoms in motor vehicle accident victims. *J Trauma Stress* 2008;21:377-84.
69. Bryant RA, Creamer M, O'Donnell ML et al. A multisite study of the capacity of acute stress disorder diagnosis to predict posttraumatic stress disorder. *J Clin Psychiatry* 2008;69:923-9.
70. Shalev AY, Videlock EJ, Peleg T et al. Stress hormones and post-traumatic stress disorder in civilian trauma victims: a longitudinal study. Part I: HPA axis responses. *Int J Neuropsychopharmacol* 2008;11:365-72.
71. Matsuoka Y, Nishi D, Nakajima S et al. The Tachikawa cohort of motor vehicle accident study investigating psychological distress: design, methods and cohort profiles. *Soc Psychiatry Psychiatr Epidemiol* 2009;44:333-40.
72. Mouthaan J, Sijbrandij M, Luitse JS et al. The role of acute cortisol and DHEAS in predicting acute and chronic PTSD symptoms. *Psychoneuroendocrinology* 2014;45:179-86.
73. Blake DD, Weathers FW, Nagy LM et al. The development of a Clinician-Administered PTSD Scale. *J Trauma Stress* 1995;8:75-90.
74. Weathers FW, Keane TM, Davidson JR. Clinician-Administered PTSD Scale: a review of the first ten years of research. *Depress Anxiety* 2001;13: 132-56.
75. Weathers FW, Ruscio AM, Keane TM. Psychometric properties of nine scoring rules for the Clinician-Administered Posttraumatic Stress Disorder Scale. *Psychol Assess* 1999;11:124-33.
76. Benjet C, Bromet E, Karam E et al. The epidemiology of traumatic event exposure worldwide: results from the World Mental Health Survey Consortium. *Psychol Med* 2016;46:327-43.
77. Buuren S, Groothuis-Oudshoorn K. MICE: multivariate imputation by chained equations in R. *J Stat Softw* 2011;45(3).
78. Rubin DB. Multiple imputation for nonresponse in surveys, Vol. 81. Chichester: Wiley, 2004.
79. Brier GW. Verification of forecasts expressed in terms of probability. *Mon Weather Rev* 1950;78:1-3.
80. Gelman A, Su Y-S, Yajima M, et al. Arm: data analysis using regression and multilevel/hierarchical models (R package, version 9.01). <http://CRAN.R-project.org/package=arm>.
81. Wolf EJ, Maniates H, Nugent N et al. Traumatic stress and accelerated DNA methylation age: a meta-analysis. *Psychoneuroendocrinology* 2018;92:123-34.
82. Sumner JA, Chen Q, Roberts AL et al. Posttraumatic stress disorder onset and inflammatory and endothelial function biomarkers in women. *Brain Behav Immun* 2018;69:203-9.
83. Duncan LE, Ratanatharathorn A, Aiello AE et al. Largest GWAS of PTSD (N=20 070) yields genetic overlap with schizophrenia and sex differences in heritability. *Mol Psychiatry* 2018;23:666-73.
84. Shalev A, Liberzon I, Marmar C. Post-traumatic stress disorder. *N Engl J Med* 2017;376:2459-69.
85. Liberzon I. Searching for intermediate phenotypes in posttraumatic stress disorder. *Biol Psychiatry* 2018;83:797-9.
86. Fonzo GA, Goodkind MS, Oathes DJ et al. PTSD psychotherapy outcome predicted by brain activation during emotional reactivity and regulation. *Am J Psychiatry* 2017;174:1163-74.
87. Logue MW, Amstadter AB, Baker DG et al. The Psychiatric Genomics Consortium Posttraumatic Stress Disorder Workgroup: posttraumatic stress disorder enters the age of large-scale genomic collaboration. *Neuropsychopharmacology* 2015;40:2287.

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